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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/757,289	DEFREES ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72-86* is/are pending in the application.

4a) Of the above claim(s) *73 and 76-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72,74,75 and 84-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/31/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicants' election with traverse of Group I, claims 72, 74, 75, 84, 85, and 86, in the reply filed on 01/10/2005 is acknowledged. The traversal is on the ground(s) that there is no serious burden to search all of the inventions of Groups I-III. This is not found persuasive because as stated in the previous Office Action the processes of Groups I-III are distinct both physically and functionally; require different process steps, reagents, and parameters; have different purposes; and produce different products. A search of all the inventions in the patent literature and the non-patent literature cannot be made without serious burden because the inventions require separate searches that have different limits, boundaries, scope, and subject matter. Because these inventions are distinct for the reasons given above and of record and have acquired a separate status in the art as shown by their divergent subject matter and classification, restriction for examination purposes is proper.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 72, 74, 75, 84, 85, and 86 are under consideration in this Office Action.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 72, 74, 75, 84-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims genus claims directed toward a genus of methods for synthesizing any polysaccharide backbone for heparin using any microorganism or plant cell that has any enzymatic system for forming UDP-GlcNAc and UDP-glucuronic acid. The scope the genus includes many enzymatic systems with widely differing enzymes of different structural, chemical, and physical characteristics. Furthermore, each genus is highly variable because a significant number of enzymatic systems containing enzymes for making UDP-GlcNAc and UDP-glucuronic acid exists.

The specification discloses and only provides a written description of a recombinant yeast or bacteria transformed with polynucleotides encoding β-G1cNAc transferase, β 1,4-glucuronylltransferase and UDP-Glc dehydrogenase. However, the specification fails to provide a written description of additional enzymatic systems for making UDP-GlcNAc and UDP-glucuronic acid.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of the necessary common features or attributes possessed by members of the genus of enzymatic systems for forming UDP-GlcNAc and UDP-glucuronic acid. Accordingly, Applicants has failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicant was in possession of the claimed invention of claims 72, 74, 75, 84-86.

Claim Rejections - 35 U.S.C. § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 72, 74, 75, 84-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujio et al. (Biosci Biotechnol Biochem. 1997 Jun;61(6):956-9) in view of De Luca et al. (Bioorg Med Chem. 1996 Jan;4(1):131-41); Nishiu et al. (Biosci Biotechnol Biochem. 1995 Sep;59(9):1750-2); Ouzzine et al. (FEBS Lett. 1994 Feb 14;339(1-2):195-9); and Lidholt et al.

(Biochem J. 1992 Oct 1;287 (Pt 1):21-9).

Fujio et al. teach a process for making pyrimidine nucleotides comprising the process steps of contacting substrates with a reaction mixture containing *C.ammoniagenes* KY13505 cells and recombinant *E.coli* strains and allowing the reaction and fermentation to proceed until pyrimidine nucleotides are produced (see entire publication, especially pp. 957-959).

Fujio et al. does not teach the process as claimed in claims [72, 74, 75, 84-86]

De Luca et al. teach a first *E.coli* strain overexpressing UDP-GlcNAc pyrophosphorylase where said first *E.coli* strain forms UDP-GlcNAc, and a second *E.coli* strain overexpressing UDP-Glc dehydrogenase where said second *E.coli* strain forms UDP-glucuronic acid (see entire publication especially Figure 2).

Nishiu et al. teach a polynucleotide encoding N-acetylglucosaminyltransferase which catalyzes the transfer of GlcNAc from UDP-GlcNAc to terminal glucuronic acid on an acceptor saccharide (see entire publication).

Ouzzine et al. teach a polynucleotide encoding UDP-glucuronosyltransferase which catalyzes the transfer of glucuronic acid from UDP-glucuronic acid to a terminal GlcNAc residue on the acceptor saccharide (see entire publication).

Lidholt et al. teach an acceptor oligosaccharides used as a polysaccharide backbone in the biosynthesis of heparin, and process steps for the formation of heparin sulfate comprising transfer of GlcNAc by GlcNAc transferase and subsequent transfer of GlcA by GlcA transferase to acceptor saccharide, action of the N-deacetylease/N-sulphotransferase on the acceptor saccharide where the N-acetyl group is exchanged for an N-sulphate group, action of C-5 epimerase (glucuronic acid 5'-epimerase) for epimerization of GlcA to iduronic acid (IdoA) residues, and action of O-sulphotransferases to form heparin sulfate (see entire publication especially Figure 10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to: modify the first *E.coli* strain overexpressing UDP-GlcNAc pyrophosphorylase taught by De Luca et al. by transformation with a polynucleotide encoding N-acetyl glucosaminyltransferase taught by Nishiu et al. to make a first recombinant *E.coli* strain having a biosynthetic system for making UDP-GlcNAc and a recombinant N-acetyl glucosaminyltransferase; modify the second *E.coli* strain overexpressing UDP-Glc dehydrogenase

taught De Luca et al. by transformation with a polynucleotide encoding UDP-glucuronosyltransferase taught by Ouzzine et al. to make a second recombinant *E.coli* strain having a biosynthetic system for making UDP-glucuronic acid and a recombinant glucuronic acid transferase; modify the process taught by Fujio et al. by replacing the mixture with the said first recombinant *E.coli* strain and the said second recombinant *E.coli* strain and replacing the substrates with acceptor oligosaccharides taught by Lidholt et al. which are used as a polysaccharide backbone in the biosynthesis of heparin; and allowing the reaction between the acceptor oligosaccharides taught by Lidholt et al. and the reaction mixture containing said said first recombinant *E.coli* strain and the said second recombinant *E.coli* strain to proceed until a heparin polysaccharide backbone is produced. One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of making a beneficial process that produces a heparin polysaccharide backbone which in turn can be used to make heparin and heparin sulfate.

Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the modified Fujio et al. process stated above comprising transfer of GlcNAc by GlcNAc transferase and subsequent transfer of GlcA by GlcA transferase to the produced heparin polysaccharide backbone, action of the N-deacetylease/N-sulphotransferase on the said produced heparin polysaccharide backbone where the N-acetyl group is exchanged for an N-sulphate group, action of C-5 epimerase (glucuronic acid 5'-epimerase) for epimerization of GlcA to iduronic acid (IdoA) residues, and action of O-sulphotransferases to form heparin sulfate as taught by Lidholt et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of making a beneficial process that produces heparin and/or heparin sulfate.

No patentable weight is given to the preamble of the process claims 72, 74, 75, 84-86 since it merely recites the purpose of these process claims. Because the process steps of the modified Fujio et al. process stated above stated above are the same as the process steps of claims 72, 74, 75, 84-86, then the modified Fujio et al. process would inherently produce the polysaccharide backbone for heparin recited in claims 72, 74, 75 and the heparin sulfate recited in claims 84-86.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

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